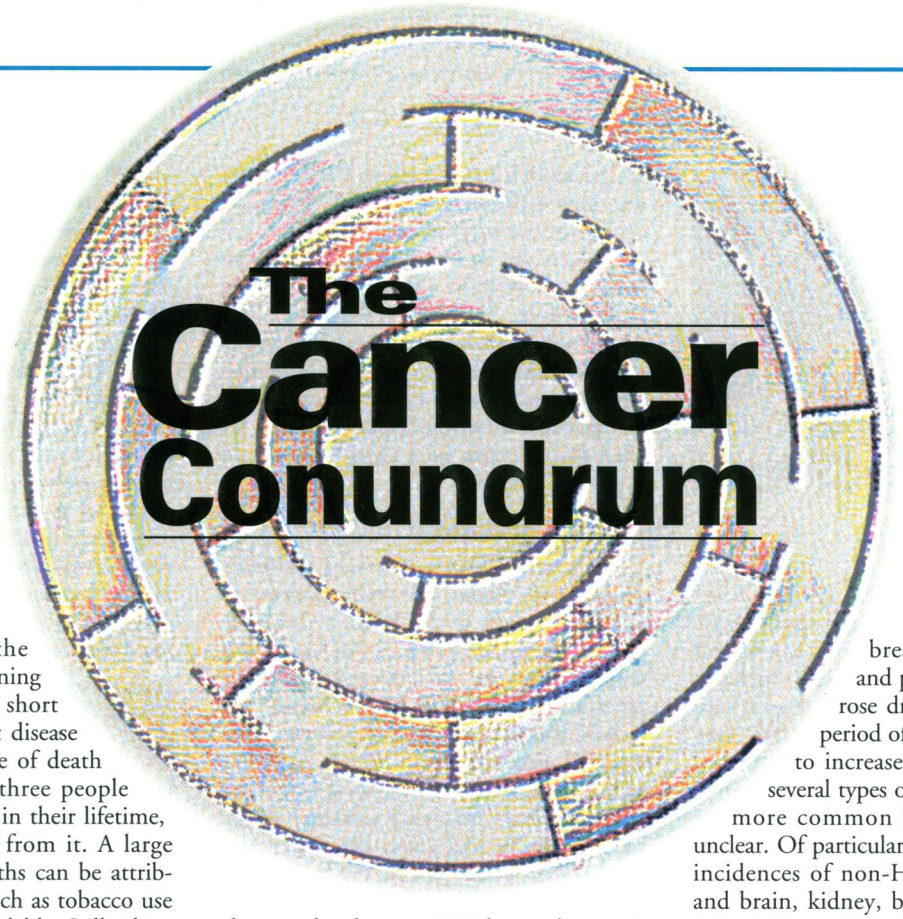
The Cancer Conundrum

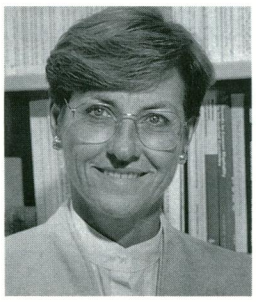


Joseph Tart

In the United States, the alarming statistics concerning cancer are that in a few short years it will surpass heart disease as the predominant cause of death in this country, one in three people will be diagnosed with it in their lifetime, and one in five will die from it. A large proportion of cancer deaths can be attributed to lifestyle factors such as tobacco use and diet and thus are avoidable. Still others may be linked to occupational and environmental exposures that individuals have little or no control over.

In an effort to reduce this enormous cancer burden, the United States mandated the National Cancer Act of 1971. More than two decades later, gains have been made but the eradication of cancer remains an elusive goal. Even when cancers caused by smoking are disregarded and the aging of the U.S. population is taken into account, an upward trend of malignancy is still evident, though researchers debate whether seeming increases in incidences are real or due to improved diagnosis, and opinions vary on cancer causation. "Whether or not the rates are rising or falling does not seem to me a debatable issue," says Philip Cole, a professor of epidemiology at the University of Alabama, Birmingham. "Some rates are rising, some are falling, some are steady. This is a factual observation. What is debatable might be whether or not the seeming rise is real, or whether or not the seeming declines are real, and what each is due to."

Cole's mention of "a factual observation" refers to the recent effort of a team of researchers at the National Cancer Institute to identify cancers accounting for rising incidence rates, quantify changes that have occurred regarding incidence from the mid-1970s to early 1990s, and contrast incidence and mortality trends to provide clues to the determinants of temporal patterns. Cancer incidence and mortality rates were collected from 1987 to 1991 and compared to those from 1975 to 1979. Findings of the study were published in the 1 February 1995 issue of the *Journal of the National Cancer Institute.*



Brooks/Glogau Studio

Susan S. Devesa—Increases in cancer incidence are not due to environment.

The team used data from the latest edition of NCI's annual update of cancer statistics, compiled by the SEER Program (Surveillance, Epidemiology, and End Results), which has monitored the occurrence of cancer and survival of patients since 1973. The update reports and summarizes cancer's impact on the U.S. population and monitors statistics to assess progress and identify areas where control efforts should be concentrated. The NCI researchers found that trends in cancer differ according to the type of disease and, although mortality rates for all cancers combined have risen among men and women, mostly due to increases in lung cancer mortality, death rates for the majority of cancers are steady or declining. Researchers attributed the declines primarily to changes in lifestyle, earlier detection of disease, and improved treatment.

The *JNCI* article also concluded that the incidence of breast cancer in women and prostate cancer in men rose dramatically during the period of the study, due largely to increased detection, and that several types of cancer are becoming more common for reasons that are unclear. Of particular concern are increased incidences of non-Hodgkin's lymphoma and brain, kidney, bladder, and testicular cancers.

The Causation Debate

Researchers have put forth a variety of theories for the increased incidence of some cancers, including a population that is growing and aging, better screening techniques, earlier diagnosis, and the impact of environmental and occupational exposure to chemicals. The latter is probably the most controversial of these theories and divides the players in the debate.

"Cancer is an important public health problem in this country," says Susan S. Devesa, team leader of the NCI study and chief of the Descriptive Studies Section of the Epidemiology and Biostatistics Program at NCI. "But, with respect to the concern that we might be having large increases in cancer incidence due to environmental influences, I think our studies show that is not the case."

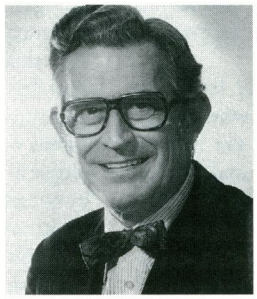
Overall, Cole agrees with Devesa, and chides those who predict an impending cancer disaster. In his February 1 editorial in *JNCI*, titled "The Evolving Picture of Cancer in America," Cole suggests that over the past 20 years the popular media and some scientific literature have implicated the pollution of the general environment as causing cancer incidence to increase. He stresses that these "pronouncements" contained sensational elements and resulted in the call for more stringent environmental regulations. Ultimately, Cole does not deny that our air

and water contain substances labeled as carcinogenic by various agencies. He does, however, challenge the validity of such evaluations. "What is not correct is that these airborne or waterborne levels of carcinogens have been shown to cause cancer in human beings," says Cole.

According to David P. Rall, retired assistant surgeon general with the Public Health Service and former director of the NIEHS, there is no such thing as proof when it comes to assessing the impact of potential environmental and occupational carcinogens on human health. "That's the real problem," Rall says. "Nobody knows how much environmental and occupational chemicals affect the overall cancer rate. Epidemiological studies have such a high threshold that it's very difficult to prove anything." With the burden of proof in mind, Rall believes that more effective epidemiology studies are needed, and he questions the contention made by Devesa and others that increased screening accounts for most of the recent increases in cancer incidence. "The increase in incidence has been steady, and if in fact this were due to better technology, the incidence should have gone up in jumps as CAT scans and magnetic resonance imaging were developed. That didn't seem to happen," he says.

According to the National Cancer Advisory Board (NCAB) in the September 1994 report, *Cancer at a Crossroads: A Report to Congress for the Nation*, "We are just beginning to understand the full range of health effects resulting from the exposure to occupational and environmental agents and factors." Consequently, the NCAB suggests the elimination or reduction of exposure to carcinogenic agents, including pesticides and other synthetic chemicals, as a priority in the prevention of cancer.

Bruce Ames, director of the Environmental Health Sciences Center at the University of California at Berkeley, believes such measures could result in substantial *increases* in the risk of cancer. Ames firmly believes that pesticides are one of the major public health advances of this century. He contends that one-quarter of the U.S. population's intake of fresh fruits and vegetables is inadequate, and that consequently their chromosomes are breaking down due to a lack of the vitamins folic acid and ascorbic acid. Ames says the elimination of pesticides would promote cancer risk because fruit and vegetable prices would increase, and fewer people would be able to buy fruits and vegetables.

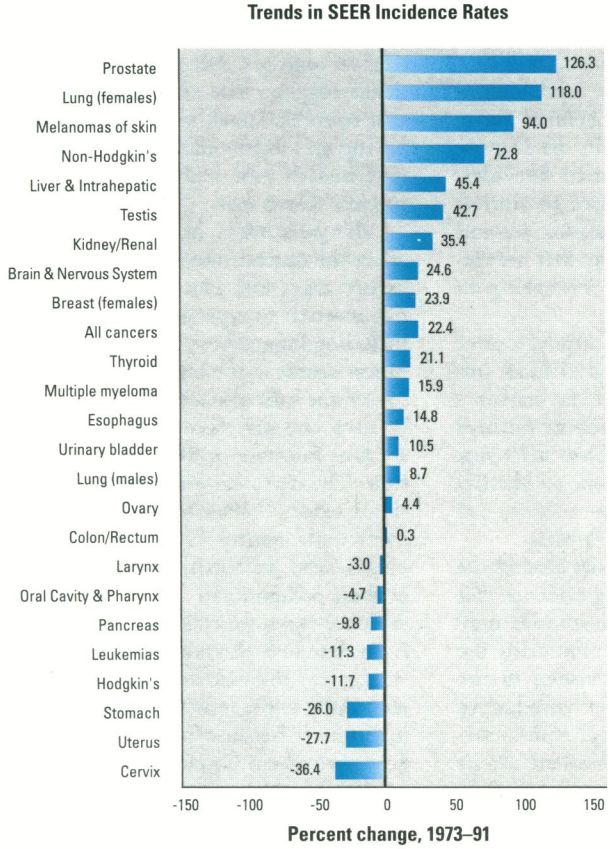


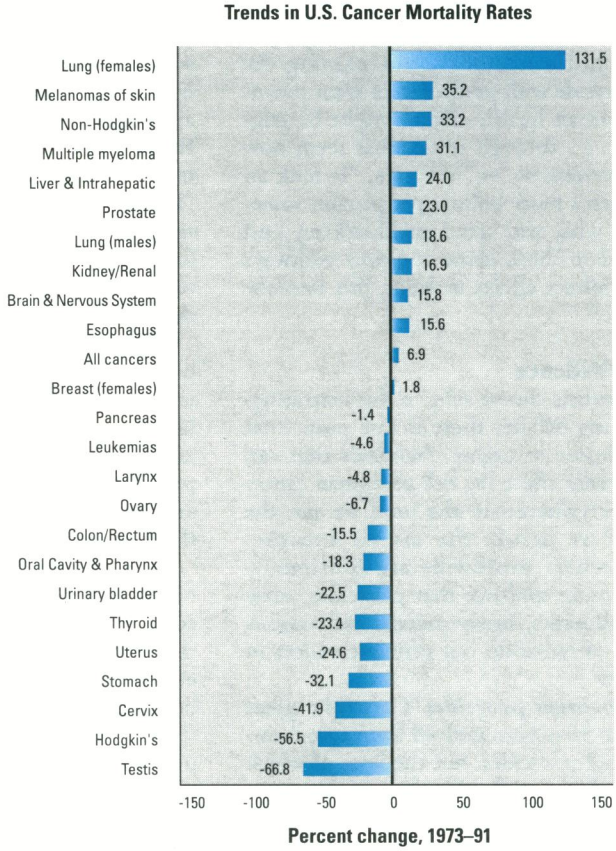
NIEHS

David P. Rall—No one knows how chemicals affect cancer rates.

In a chapter in the book, *The True State of the Planet* (Free Press, 1995), Ames writes, "Because of their unusual lipophilicity and long environmental persistence, there has been particular concern for a small group of polychlorinated synthetic chemicals, such as DDT and PCBs." Ames states that there is no convincing epidemiological evidence and little toxicological plausibility that the levels of these chemicals found in the environment are likely to be a significant contributor to cancer.

"Of course we need rules to use these chemicals, but we don't need to spend 2–5% of the gross domestic product chasing after parts per billion [levels] that are not going to have anything to do with causing cancer," says Ames. "People are getting distracted with a million hypothetical risks that aren't really risks. A lot of money is being spent because it's been hyped up that the chemical industry is giving people cancer. There are a lot of people



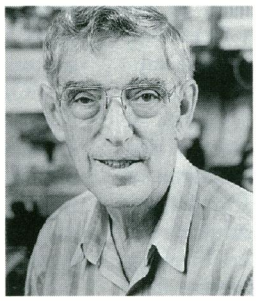


Source: *SEER Cancer Statistics Review, 1973–1991.*

that have a big self-interest in this hype, and there's really no evidence to support it; it's implausible."

Another voice that is rarely heard in the debate on cancer, but one which provides a different perspective on the impact of environmental and occupational factors on cancer, is that of the ecologist, says Sandra Steingraber. Steingraber, a biologist at Northeastern University whose focus is in community ecology, is the author of a forthcoming book on cancer and the environment. She says that ecology, a discipline that struggles to make sense of multiple effects and exposures, offers great insight into cancers because they are caused by multiple factors and are subject to a kaleidoscope of changing events.

"You miss a lot of the bigger picture of cancer if you take a kind of physics approach to it," Steingraber says. "Often very small changes are exerted over long periods of time that eventually accumulate and create very dramatic changes in the ecosystem."



UC-Berkeley

Bruce Ames—People are getting distracted by hypothetical risks.

Steingraber offers Rachel Carson as an example of a scientist whose ecological approach to wildlife biology resulted in some startling realizations that were a wake-up call to American society after World War II. "No one before her grasped the significance of . . . blanketing the countryside with pesticides, of what potential human health effects might be triggered . . . through routes that seem now very obvious to us," she says. "It took an ecologist's more holistic perspective, somebody who was used to thinking and trained to think about multiple pathways and indirect effects to bring this into the picture."

The Evidence

As scientists choose sides in this increasingly strong debate, there is one point that few choose to argue: chemicals that can potentially affect the risk of human cancer are everywhere—in the food we eat, the water we drink, the air we breathe. Researchers worldwide are continually uncovering evidence that pesticides, toxic air pollutants, heavy metals, and various forms of radiation can promote cancer in humans.

Persistent pesticides. Certainly, great benefits have been derived from agrochemicals and pesticides, not the least of which is the ability to produce large amounts of food crops at a savings of millions of dollars a year. At the same time, scientific literature is replete with evidence of the carcinogenic properties of various pesticide chemicals. For example, organophosphate insecticides have been linked with a risk for non-Hodkgin's lymphoma, and organochlorines, including DDT, have been associated with leukemia. Animal and epidemiological studies have shown an association between non-Hodgkin's lymphoma and brain and kidney cancer and exposure to pesticides or solvents such as gasoline.

Research on farmers' health has shown that though they tend to live longer and healthier lives than the general population and have impressively low rates of heart disease and other ailments, for decades farmers have exceeded the national average for certain cancers, including leukemia, multiple myeloma, non-Hodgkin's lymphoma, and cancers of the brain, prostate, stomach, skin, and lip. NCI researchers believe that such laboratory and epidemiological findings may suggest broader public health implications, as several of the malignancies associated with farmers appear to be on the rise in the general populations of several countries.

"In addition to pesticides, farmers incur chronic exposures to potentially harmful compounds, such as engine exhausts, chemical solvents, fuels, animal viruses, and sunlight," says Devra Lee Davis, a presidential appointee to the National Chemical Safety Board and a senior advisor in the Department of Health and Human Services. "Could increasing exposures to similar materials in the general population account for the fact that some cancers that are elevated in farmers are also increasing in developed countries?"

The Agricultural Health Study, a joint project of the NCI, EPA, and NIEHS, initiated in January 1993, is the nation's largest epidemiological study of farmers and their families to date. Over a 10-year period, investigators will work to identify and assess factors that may account for these cancer excesses among farmers.

In a number of laboratories around the world, researchers are finding evidence that some chemicals used in pesticides may contribute to cancer risk by mimicking the effects of the hormone estrogen in the body. Cancers that develop in reproductive tissues, such as breast, ovary, endometrium, and prostate, are dependent on an interactive network of various hormones, including estrogen, for their structural and functional development. Findings suggest that pesticides such as DDT, heptachlor, and atrazine, as well as several polycyclic aromatic hydrocarbons, petroleum byproducts, and PCBs, possess estrogenic properties.

"We are particularly concerned about materials called xenoestrogens, a number of persistent, widespread environmental chemicals that have clearly been demonstrated to disrupt the endocrine system experimentally," says Davis, who, along with colleagues Erin Blair and Joseph Fraumeni of NCI, coined the term "xenoestrogen" in 1993. "When exposed to them, the body alters the production and metabolism of its natural levels of estradiols." Davis is a key architect of the theory that xenoestrogens are a preventable cause of breast cancer. She says that evidence implicating xenoestrogens as a factor in the causation of breast cancers includes cell culture experiments, animal experiments, and human and wildlife observations.

Conclusions of recent animal studies have indicated a relationship between the level and duration of estrogen exposure and tumor development in hormonally sensitive tissues and between environmental estrogens and testicular abnormalities similar to those reported to be on the rise in men, which include not only cancers, but undescended testicles and defective sperm. Decreases in sperm quality in otherwise healthy men over the past several decades have been reported worldwide. "Taken together, this growing body of evidence suggests that environmental factors that resemble female sex hormones may be having an adverse effect on the reproductive health and well being of diverse species," Davis says.

Air pollution. Many air pollutants affect the mucous membranes of the respiratory tract and can contribute to the occurrence or aggravation of disease, including lung cancer, the leading cause of cancer deaths in the United States.

Of the tons of material emitted annually into the air, five major pollutants account for close to 98% of overall pollution. These are carbon monoxide (52%), sulfur oxides (18%), hydrocarbons (12%), particulate matter (10%), and nitrogen oxides (6%). In regard to the contribution of these pollutants to cancer, the weight of evidence varies from limited to substantial. According to Steingraber, of these five substances, it's difficult to discern which ones contribute to the growth of specific cancers in humans because people are typically exposed to them simultaneously.

"It's rare that you can go someplace in the world where you've got a lot of particulate matter but no hydrocarbon vapors, or a lot of sulfur dioxide but no particulates,"

Steingraber says. "In urban environments these substances come as a package. Therefore, the best we can do in human studies is attempt to determine if air pollution and lung cancer or air pollution and other kinds of cancers are associated."

Steingraber points out that though air pollution alone may be a weak carcinogen, it may be a significant factor in encouraging the growth and spread of cancer when mixed with exposures to other substances, such as the indoor air pollutants formaldehyde and tobacco smoke.

"Air pollution may contribute to a lot of cancers, but only because it's the straw that breaks the camel's back," she says. "There is some evidence from animal studies indicating that air pollutants, such as nitrogen dioxide, encourage more rapid growth and dissemination from cancer, perhaps by making the lungs more vulnerable to metastases from other primary tumors. The relevance of these studies to humans has yet to be shown."

Despite this uncertainty, available data indicate numerous toxic air pollutants may be important contributors to cancer incidence. These pollutants include metals such as chromium and arsenic, asbestos, products of incomplete combustion, formaldehyde, benzene, ethylene oxide, gasoline vapors, and chlorinated compounds such as chloroform, carbon tetrachloride, and trichloroethylene.

Environmental tobacco smoke. On 7 January 1992, the EPA released a report in which environmental tobacco smoke (ETS) was classified as a group A carcinogen—a category reserved for the most dangerous cancer-causing agents in humans, such as asbestos, benzene, and radon. The report, *Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders*, indicated that in 24 out of 30 independent studies, an increased risk of lung cancer from secondhand smoke was observed in nonsmokers. EPA scientists estimate that ETS causes about 3,000 lung cancer deaths each year.

ETS is the combination of sidestream smoke (smoke emitted between puffs of a burning cigarette, pipe, or cigar) and smoke that is exhaled by the smoker. ETS contains essentially all the same carcinogenic and toxic agents that have been identified in mainstream smoke inhaled by smokers. Of the 4,000 individual compounds identified in tobacco and tobacco smoke, about 60 have been identified as carcinogens, tumor initiators, and tumor promoters. Some of these compounds include tar, carbon monoxide, hydrogen cyanide, phenols, ammonia, formaldehyde, benzene, nitrosamine, and nicotine.

Illuminating Cancer at the Molecular Level

Technology is illuminating new strategies and methods for assessing cancer risk that will aid in the identification and diagnosis of the disease at its most primary foundation—the molecular level.

"People are now able to study what chemicals are doing inside cells that affects the growth control of cells," says Jeanette Wiltse, associate director for health at the National Center for Environmental Assessment at the EPA. "The difference between the way cancer assessments were done in the past and the way they're going to have to be done in the future is that we will pull this new information and technology into assessing whether a compound—a chemical—that we're looking at has carcinogenic potential or not."


EPA

Jeanette Wiltse—Molecular biology is the basis of new guidelines on risk.

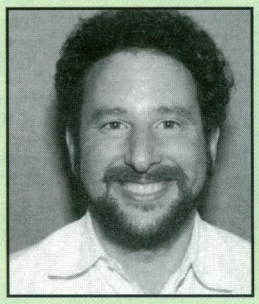
Wiltse is a member of the team responsible for updating the EPA guidelines for cancer risk assessment. The new guidelines will require regulators to incorporate such factors as how a chemical's structural features might affect its toxicity and how a chemical is absorbed, metabolized, and distributed in the body into chemical regulations. This new tack is being hailed as a major shift in the EPA's regulation of toxic chemicals.

"A whole new science has come out of the research of the last five to seven years," says Wiltse. "Our old guidelines were based on data from 10 years ago. Basically, we're updating the guidelines to take into account this new information about the molecular biology of cancer."

Currently, the most simple and straightforward conceptual approach to quantifying and qualifying causes of cancer at the molecular level entails using carcinogen–DNA adducts to identify how chemicals bind to DNA and cause mutations, explains Peter Shields, acting section chief in the Molecular Epidemiology Section of the Laboratory of Human Carcinogenesis at NCI. But Shields adds that the technology is far from simple.

In the past, the ability to measure the number of adducts in an individual's DNA provided researchers with a marker of exposure. Today, it provides much more than that. "This is where the field has evolved and matured over time," Shields says. "We understand that the process leading to cancer is quite complex, and that humans as biological creatures are well protected. The point is that we've learned these adducts are also markers of how the body handles exposure, of how it absorbs and metabolizes chemicals, how it escapes detoxification."

A further extrapolation of this approach to risk assessment is a concept Shields refers to as "interindividual variation," or the detection of subpopulations of sensitive or resistant individuals. "The body's ability to activate, detoxify, and repair itself is different from person to person," he says. "Just as the color of our eyes are different, so are our livers, and our repair mechanisms. Figuring out a way to detect these sensitive individuals and sensitive subpopulations might enable us to elucidate new causes of cancer."


NCI

Peter Sheilds—Assessing interindividual variation is a different approach to risk.

For example, the identification of specific genes and their different forms could provide researchers with clues about an individual's capacity for responding to exposures. Shields cautions that the field is young and that at this time it is considered a major achievement when scientists are able to demonstrate a direct genetically mediated effect.

"We're thinking of everyone as individuals now, and that's a fundamental difference," Shields says. "There could be subtle differences in the population that we don't know how to quantitate yet. For example, in approaching something like breast cancer, we're thinking that maybe one type of breast cancer in some women is related to one exposure and one susceptibility, and another type of breast cancer in another group of women is related to a different exposure and susceptibility."

In September 1994, researchers at the NIEHS and the University of Utah isolated *BRCA1*, a gene that may account for some inherited breast and ovarian cancers. This gene could be used to identify women who would benefit from screening for early detection of cancers. This discovery confirms the capacity of new molecular strategies for elucidating causes of cancer.

By 1964 sufficient epidemiological data on smoking and health were available to support the claim that cigarette smoking caused lung cancer, but it was not until 1986 that reports from the International Agency for Research on Cancer (IARC), the U.S. Surgeon General, and the National Research Council concluded that passive smoking caused lung cancer in nonsmokers. Over the years, numerous epidemiological studies have supported and reinforced their conclusions. Studies from the early 1970s consistently suggested that children and infants exposed to ETS experienced significantly elevated rates of respiratory symptoms and respiratory tract infections. Throughout the 1980s, epidemiological studies indicated that nonsmokers married to smokers were at an increased risk for lung cancer. In addition, studies have shown that industrial workers are especially susceptible to lung diseases due to the combined effects of cigarette smoke and exposure to certain toxic substances present in the workplace.

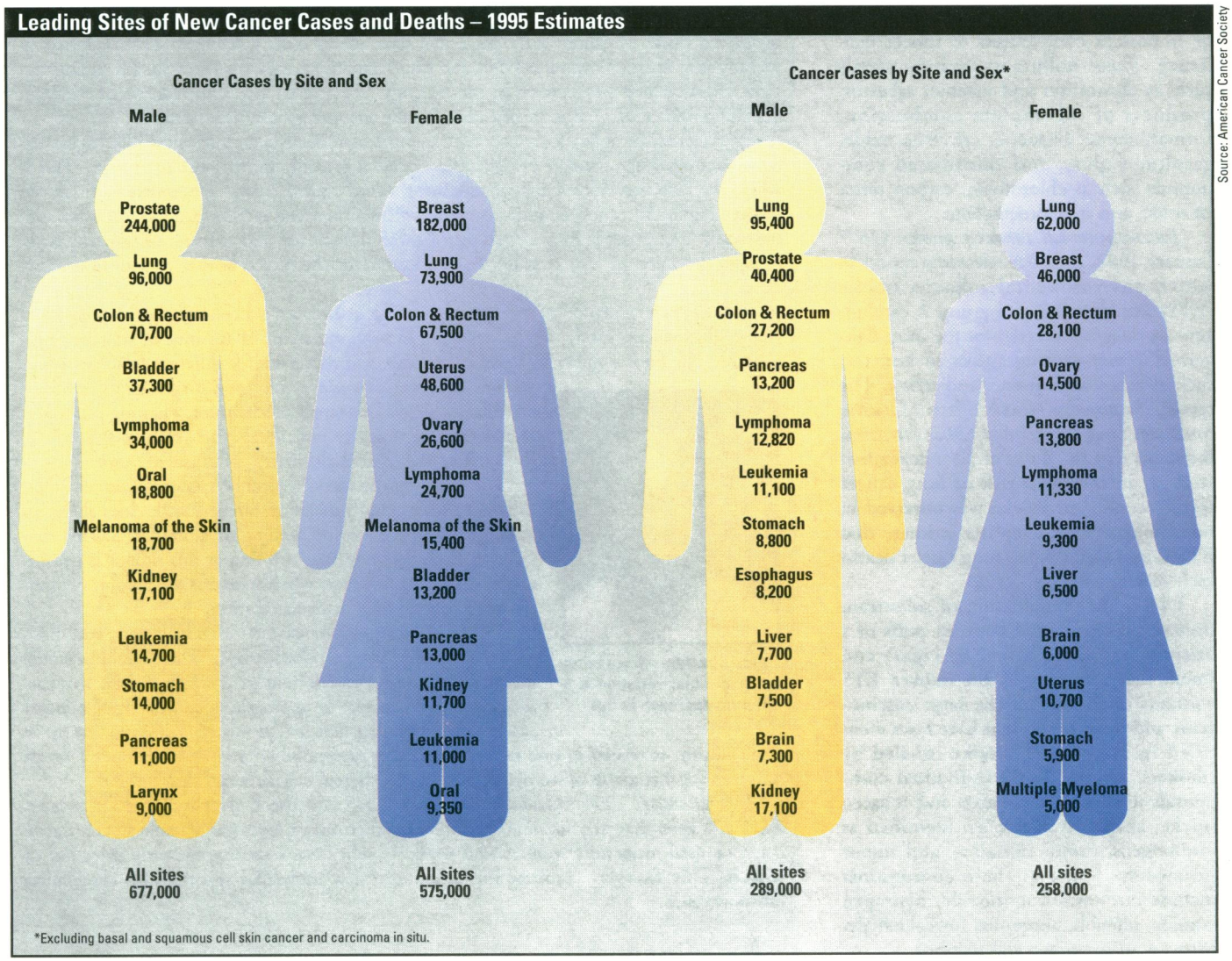
Metals. The EPA and IARC classify arsenic as a carcinogen for which there is sufficient epidemiological evidence to support a causal association between exposure and skin cancer. Arsenic, a naturally occurring, toxic metal, is released into the environment naturally by solubilization from geologic formations into water supplies. It is also released into occupational and community environments by such activities as nonferrous ore smelting and combustion of fuels containing arsenic.

According to Janice Yager and John Wiencke in a 1993 supplement to *Environmental Health Perspectives* (vol. 101, no. 3), studies of occupational exposure to high concentrations of arsenic in air at copper smelters and community exposure to arsenic in drinking water indicate an increased risk of lung and skin cancer, respectively. These authors also reported that exposure to arsenic via drinking water in Taiwan may have lead to increases in cancer at other sites, such as the bladder and kidney, and that epidemiological studies have indicated synergism between arsenic exposure and cigarette smoking in smelter workers in the induction of lung cancer.

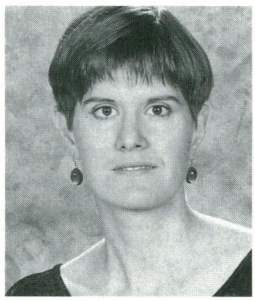
Some studies have indicated an association between exposure to inorganic arsenic and the development of lymphoma, lung, bladder, and skin cancers. Such effects may be due to arsenic acting in concert with other substances in the environment. Results of animal studies also support the theory that arsenic acts with other agents to alter or enhance carcinogenesis.

Cadmium is ubiquitous in the environment. Its most common natural form is cadmium sulfide, which is generally complexed with zinc, lead, copper, or iron, and is recovered as a by-product from the processing of these ores. The general public may be exposed to cadmium predominantly through contaminated food and water and by inhalation of cigarette smoke.

There have been numerous reports of the acute and chronic effects of cadmium in humans following accidental or occupa-



tional exposures. Various health effects have also been reported in experimental animals administered cadmium by injection, ingestion, and inhalation. The idea that cadmium might cause cancer in humans was raised in 1967 when four men who had worked in a factory making nickel–cadmium batteries died of prostate cancer. Although the information on the carcinogenicity of cadmium is incomplete, epidemiological studies during the last few years have provided further support that cadmium is carcinogenic to the lung, but not to the prostate.



Northeastern University

Sandra Steingraber—Ecology offers a holistic perspective on cancer causation.

In 1987, IARC, in its *Monograph on the Evaluations of Carcinogenicity,* reviewed a number of epidemiological studies on occupational exposure to cadmium and lung and prostatic cancer and concluded that long-term occupational exposure to cadmium may contribute to lung cancer. Confounding exposures to arsenic, nickel, and possibly other respiratory carcinogens, including cigarette smoking, prevented a more definitive conclusion.

Radioactivity. Many adverse health effects have been observed as a result of exposure to various forms of radiation, including ionizing, ultraviolet, and electromagnetic. Exposure to high levels of radiation can increase the risk of developing cancer, though a radiation-induced cancer is often indistinguishable from cancer caused by other factors, making it very difficult to pinpoint radiation as the cause of cancer.

The cancer risk associated with exposure to high levels of ionizing radiation is among the best understood of any relationship involving environmental agents and cancer. X-rays, gamma rays, radioactive materials in rocks and soil, radioactive isotopes, and coal burning are all examples of ionizing radiation.

A National Institutes of Health Fact Sheet published in 1994 cites historical data on the implications of human exposure to radiation. The adverse effects of high doses of radiation were seen shortly after the discovery of radioactivity in the 1890s. In 1902, skin cancers were reported in scientists studying radioactivity. A 1931 report described cases of bone cancer in women who wet their brushes on their tongues to get a good "point" for painting radium on watch dials. The role of radiation in human leukemia was first reported in 1944 in physicians and radiologists. The carcinogenic potential of X-rays was confirmed through epidemiological data, especially data on victims of nuclear bombs in Hiroshima and Nagasaki.

Additional information has been gleaned from studies on the health effects of radon in uranium miners. Radon is found outdoors and in all dwellings as a result of the decay of uranium. Radon's carcinogenicity is attributable chiefly to its short-lived, radioactive, alpha-emitting daughters, polonium-218 and polonium-214. Radon emanates as a toxic gas from the soil and from building materials of terrestrial origin, such as stone, bricks, and concrete.

As reported by Jonathan M. Samet and colleagues in the August 1991 issue of the *Journal of the American Medical Association,* epidemiological studies initiated in the 1950s and later, provide convincing evidence that radon causes lung cancer in miners. By the mid-1980s, it was widely recognized that radon was present in homes and other dwellings, sometimes reaching concentrations comparable to levels in uranium mines. When ventilation is restricted, radon may accumulate in concentrations substantially higher than those prevailing outdoors.

Studies of lung cancer risk from indoor radon exposures are inconclusive, according to *Radon and Lung Cancer Risk: A Joint Analysis of 11 Underground Miners Studies,* a collaborative effort involving scientists from all over the world, published in 1994. Nonetheless, based on evidence gathered from studies of miners, the NCI has estimated that residential radon may cause as many as 15,000 deaths from lung cancer in the United States annually (see *EHP* vol. 103, no. 10). This estimate includes lung cancers ascribed to radon exposure alone and those attributed to a combination of radon exposure and smoking. Available data suggest that the risk of lung cancer from exposure to radon and smoking are at least additive, if not multiplicative.

According to the NCI, skin cancer is the most common type of cancer in the United States. Current estimates suggest that 40–50% of Americans who live to age 65 will have skin cancer at least once.

Ultraviolet (UV) radiation from sunlight is the major cause of skin cancers, including malignant melanoma. Artificial sources of UV radiation, such as sunlamps and tanning booths, can also cause skin cancer. There is extensive epidemiological evidence supporting a direct role of sunlight in skin cancer. The evidence suggests that intermittent exposures are important in melanoma, whereas cumulative or occupational exposures are more closely related to nonmelanoma skin cancer.

Also of serious concern regarding the rising incidence rates of skin cancers is the depletion of the ozone layer, caused by man-made chlorofluorocarbons (CFCs). Although their manufacture and import into the United States will be illegal in January 1996, these extraordinarily inert chemicals have been used in numerous commercial products, such as aerosols and refrigerants. According to Steingraber, the rise of refrigeration, made possible by CFCs, resulted in a strange twist of fate: healthier eating habits and lower rates of stomach cancer, coupled with ozone destruction and its accompanying rise in melanoma and nonmelanoma skin cancers.

"Thanks to refrigeration, we are able to eat fresh fruits and vegetables, and foods that aren't preserved with nitrites, or by smoking, pickling, or salting," Steingraber says. "We've reduced our exposure to these toxic substances that were commonly used to preserve food 50 to 100 years ago, and these changes may be behind the recent decline in stomach cancer. Ironically, the unforeseen consequence is a potential epidemic of skin cancer."

In a May 1989 risk assessment document, the EPA predicted that without controls on CFC production, a 40% depletion of ozone would occur by the year 2075. The agency further concluded that for every 1% decrease in ozone, there will be a 2% increase in the more damaging UV-B wavelengths reaching the earth's surface. Such an increase in UV-B penetration is predicted to result in an additional 1–3% increase per year in nonmelanoma skin cancer.

DHHS

Devra Lee Davis—Environmental factors may be having adverse effects on reproductive health.

While there is strong evidence that radiation from sources such as radiotherapy can increase the risk of tumors of the nervous system, the picture is less clear concerning risks posed by low doses of ionizing radiation or EMFs. Characterized as nonionizing radiation, EMFs are emitted from devices such as power lines, transmitters, and common household items such as televisions, clocks, computers, electric blankets, and microwave ovens.

More than a decade ago, epidemiological studies suggested that exposure to electromagnetic fields (EMFs) in occupational

and residential environments might cause cancer. Reports have indicated associations between exposures to low-frequency (50–60 Hertz) fields and rare cancers, principally leukemia, and to cancers that are currently increasing in the U.S. population, including brain and breast cancer.

Acute lymphocytic leukemia (ALL), which accounts for 85% of all childhood leukemias in the United States, has been linked to EMF exposure. A collaborative study between NCI and the Children's Cancer Group, headquartered at the University of California at Pasadena, is being conducted to evaluate the risk of ALL associated with a wide range of factors, including EMF exposure. Data from the study will be used to estimate the amount of prenatal and lifetime EMF exposure. EMFs have also been linked to cancers of the nervous system and brain. Evidence on the carcinogenicity of EMFs has thus far been inconsistent, but the potential health hazards of EMF exposure remain an active area of cancer research.

Investigators at the University of North Carolina at Chapel Hill's School of Public Health recently assessed the relationship between EMFs and breast cancer mortality in female electrical workers in the United States. Their findings, published in the June 1994 issue of *JNCI*, indicated that women in electrical occupations have a nearly 40% higher mortality risk from breast cancer than women in the labor force without occupational exposure to strong electric or magnetic fields. Though researchers at NCI disputed those findings, David Savitz, a professor of epidemiology in the School of Public Health at UNC, and a member of the investigation team, says that the increasing incidence of breast cancer is justification for addressing the hypothesis. "Given the numbers affected and how little we actually know about breast cancer, at least in terms of ways that we can prevent it, we need to be pretty open minded about what might be going on here," says Savitz.

Breast cancer is the most frequently diagnosed cancer in women in the United States today. As pointed out in the *SEER Cancer Statistics Review 1973–1991*, the gradual, long-term increase in breast cancer incidence seen over the past few decades is difficult to explain. With the worldwide annual incidence of breast cancer cases expected to reach one million by the end of this century, a causal relationship between EMFs and breast cancer would have broad implications.

In light of the fact that overall cancer incidence rates are rising, most for reasons that are unclear, Savitz's advice to remain open minded is sound. It seems apparent that lifestyle choices can either protect against or promote the onset of cancer. There is also ample evidence illuminating the role that exposure to various natural and man-made environmental substances play in cancer. Ultimately, elucidating the cause of cancer and protecting people against its encroaching shadow will entail vigilant research and clarification of the interplay of environmental and genetic factors.

Kate Cahow